UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/857,651	08/27/2001	Tatsuji Seki	9150-0009.10	1049

22918 7590 12/22/2003

PERKINS COIE LLP
P.O. BOX 2168
MENLO PARK, CA 94026

EXAMINER	
KRUSE, DAVID H	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 12/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/857,651	SEKI ET AL.	
	Examiner	Art Unit	
	David H Kruse	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *13 and 14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 June 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group II, claims 8-11 in the Response filed 29 September 2003 is acknowledged. Upon reconsideration of the requirement for restriction, the Examiner has rejoined Group I, claims 1-7, and Group III, claim 12.

Applicant should note that the prohibition against double patenting rejections of 35 U.S.C. § 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

2. Claims 13 and 14 are withdrawn from further consideration pursuant to 37 CFR § 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the Response filed 29 September 2003.

3. This application contains claims 13 and 14 drawn to an invention nonelected without traverse in the Response filed 29 September 2003. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR § 1.144) See MPEP § 821.01.

Specification

4. The abstract of the disclosure does not commence on a separate sheet in accordance with 37 CFR § 1.52(b)(4). A new abstract of the disclosure directed to the claimed invention is required and must be presented on a separate sheet, apart from any other text.

5. The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. See the Preliminary Amendment filed 7 June 2001, page 1. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

6. At page 1, the first sentence of the specification as amended on 7 June 2001, the phrase "claims priority to application no." should read -- is the National Stage of International Application No --.

Claim Rejections - 35 USC § 101

7. 35 U.S.C. § 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claims 8 and 11 are rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter. The instant claims are non-statutory subject matter because they do not denote the hand of man, and because a product of nature inherently has the properties of the claimed plant cell and regenerated plant. As evidence, the Examiner cites Takahashi *et al*, Biochemistry 1986, 25:388-395, which discloses that Sycamore cells inherently have the properties of the claimed plant cells and plant, in particular the glycoprotein laccase (see Figure 3 on page 391). It is

suggested that the instant claims be amended to be directed to transgenic plant cells and plants, transformed to have the claimed sugar chain adding mechanism.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

10. Claims 1-7, 9-11 and 12 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

At claim 1, lines 1-2, the limitation "having a human-type sugar chain" is indefinite and is relative depending upon what glycoprotein is glycosylated, and thus does not state the metes and bounds of the claimed invention. At lines 3 and 5, "obtained" renders the claim indefinite because it does not denote a positive method step of manufacture, the limitation -- produced -- is suggested. The limitations "the gene of glycosyltransferase" at line 4, and "the gene of an exogenous glycoprotein" at lines 4-5, lack proper antecedent basis within the claim.

At claim 2, line 2, "capable of conducting a transfer reaction of" renders the claim indefinite because it is unclear if the enzyme actually has the recited activity. The limitation -- which transfers -- is suggested.

At claim 3, line 2, "with a human-type sugar chain" is indefinite for the reasons given above for claim 1.

At claim 7, line 2, "the glycoprotein contains neither fucose nor xylose" is indefinite because "a human-type sugar chain" does not inherently contain fucose or xylose, hence the metes and bounds of the claimed invention are unclear.

At claim 9, lines 2-3, "capable of conducting a transfer reaction of" renders the claim indefinite because it is unclear if the enzyme actually has the recited activity. The limitation -- which transfers -- is suggested. At line 5, "can enhance the first enzyme" renders the claim indefinite because it is unclear what the metes and bounds of this limitation are as directed to "can enhance".

Claim 10 is indefinite because it is unclear how the "second enzyme" β1,4-Galactosyltransferase, which has the activity of the "first enzyme" at claim 9, would "enhance" itself, hence the metes and bounds of the claimed invention are unclear.

At claim 12, line 2, "mammalian-like glycoprotein" is indefinite for the reasons give for claim 1, because the limitation appears relative and does not state the metes and bounds of the claimed invention. In addition, "comprising neither fucose or xylose" is indefinite because "mammalian-like glycoproteins" do not inherently comprise either sugar.

11. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 1-12 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant claims a method of manufacturing a glycoprotein having a human-type sugar chain comprising transforming a plant cell with a gene encoding a glycosyltransferase, which transfers a galactose residue to a non-reducing terminal acetylglucosamine residue, and a gene encoding an exogenous glycoprotein. Applicant also claims a plant cell having a sugar chain adding mechanism that can conduct a transfer reaction of a galactose residue to a non-reducing terminal acetylglucosamine residue.

Applicant describes a method of manufacturing a glycoprotein in a transgenic plant having terminal galactose residues in the N-glycosylation portion of a glycoprotein comprising transforming said plant with a transgene encoding a mammalian β1,4-galactosyltransferase, and a plant transformed therewith which also comprises a transgene encoding an exogenous glycoprotein, horseradish peroxidase (pages 20-38 of the specification).

Applicant does not describe a method of manufacturing comprising transforming a plant cell with other glycosyltransferase encoding nucleic acids as broadly claimed. In addition, Applicant does not describe a recombinant plant, or portion thereof, that produces mammalian-like glycoproteins comprising neither fucose nor xylose as in claim 12 (see Figure 20).

Hence, it is unclear from the instant specification that Applicant was in possession of the invention as broadly claimed.

See also, MPEP § 2163 which states that the claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence. In the instant case, the claims are drawn to a method comprising transforming a plant cell with a nucleic acid encoding a glycosyltransferase wherein such a function does not inherently produce a human-type sugar chain on a glycoprotein.

13. Claims 1-12 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for a method of manufacturing a glycoprotein in a transgenic plant having terminal galactose residues in the N-glycosylation portion of a glycoprotein comprising transforming said plant with a transgene encoding a mammalian β1,4-galactosyltransferase, and a plant transformed therewith which also comprises a transgene encoding an exogenous glycoprotein, does not reasonably provide enablement for a method of manufacturing a glycoprotein having a human-type sugar chain comprising transforming a plant cell with any gene encoding a glycosyltransferase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant claims a method of manufacturing a glycoprotein having a human-type sugar chain comprising transforming a plant cell with a gene encoding a glycosyltransferase, which transfers a galactose residue to a non-reducing terminal acetylglucosamine residue, and a gene encoding an exogenous glycoprotein. Applicant also claims a plant cell having a sugar chain adding mechanism that can conduct a transfer reaction of a galactose residue to a non-reducing terminal acetylglucosamine residue.

Applicant teaches a method of manufacturing a glycoprotein in a transgenic plant having terminal galactose residues in the N-glycosylation portion of a glycoprotein comprising transforming said plant with a transgene encoding a mammalian β1,4-galactosyltransferase, and a plant transformed therewith which also comprises a transgene encoding an exogenous glycoprotein, horseradish peroxidase (pages 20-38 of the specification).

Applicant does not teach a method of manufacturing comprising transforming a plant cell with other glycosyltransferase encoding nucleic acids as broadly claimed. In addition, Applicant does not teach a recombinant plant, or portion thereof, that produces mammalian-like glycoproteins comprising neither fucose nor xylose as in claim 12 (see Figure 20).

In re Wands, 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988) lists eight considerations for determining whether or not undue experimentation would be necessary to practice an invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of

working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims.

Applicant provides limited guidance on how to make and use transgenic plants comprising a transgene encoding a glycosyltransferase as broadly claimed. Applicant teach how to make and use a transgenic plant comprising a mammalian β1,4-galactosyltransferase to produce glycoproteins having terminal galactose residues on the N-glycosylations. Applicant does not provide guidance on how to make and use the genus of transgenic plant comprising other glycosyltransferases to produce what Applicant refers to as "human-type sugar chain" or "mammalian-like glycoproteins". The art teaches that mammals, including humans, have genes encoding a myriad of glycosyltransferases involved in glycoprotein synthesis (see Dinter and Berger 1995, The regulation of cell- and tissue-specific expression of glycans by glycosyltransferases, in Glycoimmunology, Alavi and Axford (eds), Plenum Press, New York, pp 53-82, see especially Table 1 on pages 55-57). Dinter and Berger also teach that "human-type sugar chain" or "mammalian-like glycoproteins" encompass a vast variety of combinations of polysaccharides, and that such limitations do not inherently teach the structure of the claimed invention (see Tables 2 and 3 on page 58).

Applicant does not teach how to make and use the plant cell transformed with nucleic acids encoding Mannosidase I, Mannosidase II, and N-acetylglycosaminyltransferase I (GlcNAcI), at claim 10. Applicant does not teach how to make and use a transgenic plant wherein the glycoprotein comprises neither fucose nor

xylose, in fact Applicant's example shows that these sugars are present on a proportion of the glycoproteins synthesis by the exemplified transgenic plant (Applicant's claim 7, see Figure 20 of the instant specification).

Therefore, given the limited teachings by Applicant, the nature of the claimed invention and the teaching of the art at the time of Applicant's invention, it would have required undue trial and error experimentation by one of skill in the art at the time of Applicant's invention to transform a plant cell with a myriad of nucleic acids encoding glycosyltransferases such that said plant produces glycoproteins that have "human-type sugar chain" or "mammalian-like glycoproteins" as broadly claimed.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
> If a copy of a provisional application listed on the bottom portion of the accompanying Notice of References Cited (PTO-892) form is not included with this Office action and the PTO-892 has been annotated to indicate that the copy was not readily available, it is because the copy could not be readily obtained when the Office action was mailed. Should applicant desire a copy of such a provisional application, applicant should promptly request the copy from the Office of Public Records (OPR) in accordance with 37 CFR 1.14(a)(1)(iv), paying the required fee under 37 CFR 1.19(b)(1). If a copy is ordered from OPR, the shortened statutory period for reply to this Office action will not be reset under MPEP § 710.06 unless applicant can demonstrate a substantial delay by the Office in fulfilling the order for the copy of the provisional application. Where the applicant has been notified on the PTO-892 that a copy of the provisional application is not readily available, the provision of MPEP § 707.05(a) that a copy of the cited reference will be automatically furnished without charge does not apply.

15. Claims 1-7 are rejected under 35 U.S.C. § 102(e) as being anticipated by Umana *et al*, U.S. Patent 6,602,684, issued 5 August 2003, filed 20 August 1999, and claims priority to US Provisional Application 60/082,581, filed 20 April 1998.

Claim 7 is included because the Examiner, for the purposes of the instant rejection, interprets the claim as encompassing a method wherein some of the produced glycoproteins do not contain fucose or xylose.

Umana discloses a method comprising transforming a plant cell with recombinant plasmid expression vectors containing the coding sequence of a protein of interest and the coding sequence of the glycoprotein-modifying glycosyl transferase (column 12, lines 61-67). Umana discloses that the protein of interest encompasses antibodies and antibody fragments (column 5, line 56). Umana discloses that the glycoprotein-modifying glycosyl transferase encompasses GalT (β1,4-galactosyltransferase), which transfers a galactose residue to the non-reducing terminal acetylglucosamine residue (column 5, line 41). The method of Umana would inherent have the function at Applicant's claims 4-7, because depending upon what protein of interest is introduced into the plant cell, the glycosylation would have an outer sugar chain configuration that is straight or branched, or wherein the branched sugar chain portion has a mono-, bi-, tri- or tetra configuration. In addition, the limitations at Applicant's claim 7 would be inherent in the method disclosed by Umana. Hence, all of the claim limitations have been previously disclosed by Umana *et al*.

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. Claims 8-12 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Umana *et al*, U.S. Patent 6,602,684, issued 5 August 2003, filed 20 August 1999, and claims priority to US Provisional Application 60/082,481, filed 20 April 1998, in view of Hein *et al*, U.S. Patent 5,959,177, filed 3 May 1996.

Claim 12 is included because the Examiner, for the purposes of the instant rejection, interprets the claim as encompassing a recombinant plant wherein some of the produced glycoproteins do not contain fucose or xylose.

The teachings of Umana *et al* are discussed above. Umana also teaches that multiple transgenes encoding glycosyltransferases can be transformed into the host plant cell, including mannosidase II (Man II), and that it is preferable to coexpress GalT with Man II (column 9, lines 43-60).

Umana *et al* do not specifically teach a plant cell or plant transformed to have a sugar chain adding mechanism, which can conduct a transfer reaction of a galactose residue to a non-reducing terminal acetylglucosamine residue.

Hein *et al* teach transgenic plants transformed to produce antibody molecules (claims 6-12). Hein *et al* teach that the expressed antibody molecules have a core N-glycosylation similar to mammals (column 23, lines 15-18).

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the teachings of Umana *et al* using the teachings of Hein *et al* to produce transgenic plant cells having a sugar chain adding mechanism which can conduct a transfer reaction of a galactose residue to a non-reducing terminal acetylglucosamine residue as claimed by Applicant. In addition, it would have been obvious, given the teachings of Umana *et al* as discussed supra, to transform said plant cell with other nucleic acids encoding other glycosyltransferases such as Mannosidase II. Given the success of Hein *et al* to produce a transgenic plant cell and plant that expresses an antibody glycoprotein, one of ordinary skill in the art at the time of Applicant's invention would have had a reasonable expectation of success in also introducing a GalT encoding nucleic acid. Umana *et al* motivates one of ordinary skill in the art to combine the expression of antibody genes and glycosyltransferase genes, especially GalT in a host cell expression system as discussed supra.

Conclusion

18. No claims are allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David H. Kruse, Ph.D. whose telephone number is (703) 306-4539, **(571) 272-0799 after 6 January 2004**. The examiner can normally be reached on Monday to Friday from 8:00 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Amy Nelson can be reached at (703) 306-3218, **(571) 272-0804 after 6 January 2004**. The fax telephone number for this Group is (703) 872-9306 Before Final or (703) 872-9307 After Final.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group Receptionist whose telephone number is (703) 308-0196.

David H. Kruse
AU 1638

David H. Kruse, Ph.D.
9 December 2003